

Amendments to the Specification:

Please replace the paragraph beginning on page 11, line 16 with the following amended paragraph:

Figure 3 shows the epitope analysis of the antibody according to the invention.

(A) Spot analysis using a complete set of tridecamer peptides which are derived from the extracellular part of the CD30 molecule after incubation with the antibody according to the invention, followed by marked reagents which recognise this.

(B) Analysis of the epitope of the antibody according to the invention by substitution of every individual residue of the sequence in Spot 74 (left column, identical peptides as controls) with all 20 L amino acids (upper line) (SEQ ID NO:12, and residues 1-12, 2-13, 1-11, 2-12, 3-13, 1-10, 2-11, 3-12, 4-13, 1-9, 2-10, 3-11, 4-12, 5-13, 1-8, 2-9, 3-10, 4-11, 5-12, and 6-13, respectively, of SEQ ID NO:12).

Please replace the paragraph beginning on page 12, line 16 with the following amended paragraph:

A chimerized CD30 antibody, as produced by the stored cell line DSZ1, is based on the constant regions of the human IgG1 κ chain and the variable regions which code the antigen binding site for the CEPDY epitope of CD30. The latter V genes can be isolated with the following primers:

A-C κ : 5' AGATGGATACAGTTGGT (SEQ ID NO:1); A-C $H1$: 5'
GGGGCCAGTGGATAGAC (SEQ ID NO:2);
B $NotI$: 5' GCGCGGCCGCGGAGG (SEQ ID NO:3);
C $NotI$: 5' GCGCGGCCGCGGAGGGCCCCCCCCCCCC (SEQ ID NO:4);
D-C κ _{EcoRI}: 5' GGAATT CGGATACAGTTGGTGCAGC (SEQ ID NO:5);
D-C $H1$ _{EcoRI}: 5' GGAATT CGTGGATAGACAGATGGG (SEQ ID NO:6);

E-_{κSal1}: 5' GATCGTCGACGGAAATGCATCAGACCAGCATGGC (SEQ ID NO:7);
E-H_{Sal1}: 5' CATAGTCGACAATACGATCAGCATCCTCTCCACAG (SEQ ID NO:8);
F-_{κNot1}: 5' ATCAGCGGCCGCACTTAACAAGGTTAGACTTAGTG (SEQ ID NO:9);
F-H_{Not1}: 5' GATAGCGGCCGCATGCATTAGAATGGGAGAAGTTAGG (SEQ ID NO:10);

whereby the isolated region includes the rearranged genomic VDJ region, including the original signal peptide, signal peptide intron and the authentic splice points. A V_L and a V_H clone without mutations or irregular sequences which derive from the myeloma fusion cell line were selected for cloning into the eukaryotic expression vectors pUHW_κ and pUHW_γ (available from Dr. U. Weidle, Roche, Penzberg), whereby they contained the human κ or C_H 1-3 gene segments. After stable cotransfection into the mice myeloma cell line Sp2/0-Ag14 and selection with G418, the transfecants secreted between 50 ng/ml-150 ng/ml of the antibody. For cleaning and conjugation of this chimerized antibody, this antibody was produced in large quantities by the transfected cells being placed in a hollow fibre system. After further selection with the "limiting dilution" method, partly using G418, the cells produce approx. 20 µg/ml in a conventional cell culture. In hollow fibre systems, this value is not less than 100 µg/ml and may reach up to 500 µg/ml.

Please replace the paragraph beginning on page 15, line 8 with the following amended paragraph:

The mapping of the epitope to which the antibody according to the invention binds showed that this binds to a peptide sequence which occurs twice in the extracellular domain of CD30. The antibody secreted by the cell line DSZ1 according to the invention showed two strong signals with peptides derived from CD30 (cf. Figure 3): Spot 16 (with the sequence ⁶⁴DCRKQCEPDYYLD⁷⁶ (SEQ ID NO:11)) and Spot 74 (²³⁸GDCRKQCEPDYYL²⁵⁰ (SEQ ID NO:12)). An extensive mapping of the epitope using substitution analysis gave the amino acid residue CEPDY as the core sequence for the interaction. Both epitopes bind the antibody secreted by the cell line according to the

Appl. No. 10/612,832
Amdt. dated June 15, 2004
Preliminary Amendment

PATENT

invention and the binding was not lost if only one of the epitopes was mutated, whilst mutation in both epitopes led to the loss of the antibody recognition.

Please insert the accompanying paper copy of the sequence listing, pages 1-5, at the end of the application.